REMARKS

Claims 5-12, 18, 22, 25-27, 30-35, 37, 43-50, 56, 63, and 64 are pending in the present application. By the present Communication, no claims have been added, canceled, or amended. Accordingly, claims 5-12, 18, 22, 25-27, 30-35, 37, 43-50, 56, 63, and 64 will be under consideration.

Rejections under 35 U.S.C. §103

Applicants respectfully traverse the rejection of claims 5-12, 18, 22, 25-27, 30-35, 37, 43-50, 56, 63, and 64 under 35 U.S.C. §103(a) as allegedly being unpatentable over Cox III, et al. (U.S. Pat. No. 6,608,183; hereinafter, "Cox") in view of Wild, et al. (U.S. Pat. No. 6,130,318; hereinafter, "Wild"). The recent U.S. Supreme Court decision in the KSR International v. Teleflex Inc. (82 USPQ2d 1385), modified the standard for establishing a prima facie case of obviousness. Under the KSR rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

The Office Action alleges that Cox discloses mutants of the growth hormone family, wherein specific amino acids are substituted with the amino acid cysteine, using site directed mutagenesis, then covalently coupling a polymer via the cysteine residue. However, Cox does not teach modified IL-4 muteins, wherein the specific amino acids 37, 38, or 104 are cysteine or wherein the IL-4 muteins are antagonists that inhibit IL-4 mediated processes. (Office Action, page 4). The Office Action relies upon Wild for allegedly disclosing several human IL-4 mutant proteins in which specific amino acid residues are modified to generate antagonists of IL-4. According to the Office Action, Wild does not teach specific mutations at positions 37 or 104,

but it does teach that modifying amino acid residues 38 and 105 results in an IL-4 antagonist that antagonizes IL-4 activity. (Office Action, page 5).

Applicants respectfully submit that Wild is absolutely silent with regard to replacing the amino acid residues at positions 38 and 105 with aspartic acid for any purpose other than altering the native glycosylation pattern of the polypeptide. (Wild, col. 6, lines 11-12). More specifically, Example 1 of Wild, entitled, "Removal of potential N-glycosylation sites in hIL4 mutant proteins," discloses that,

> two asparagine-coupled glycosylation sites are present at amino acid positions 38 and 105 in the natural hIL-4 amino acid sequence. The corresponding codons in the structural gene can be replaced with those for aspartic acid. This prevents N-glycosylation of the resulting hIL-4 mutant protein when its gene is expressed in yeast strains. (Wild, col. 9, line 60 to col. 10, line 3).

Accordingly, Wild fails to disclose that substituting the amino acid residues at positions 38 or 105 with any residue other than aspartic acid, and specifically fails to mention cysteine, will remove the N-glycosylation site. Applicants further submit that Cox is absolutely silent with regard to substituting an N-glycosylation site with a cysteine residue for coupling to a polymer in an IL-4 mutein. Specifically, Cox discloses that, "N- and O-linked glycosylation sites in the proteins are preferred sites for introducing cysteine substitutions either by substitution for amino acids that make up the sites *or, in the case of N-linked sites, introduction* of cysteines therein." (Cox, col. 9, lines 12-17, emphasis added). In other words, Cox discloses that when the protein has an N-linked glycosylation site, as in the IL-4 muteins of the present invention, *introduction* of a cysteine residue within the glycosylation site, rather than *substitution* of the amino acid residue at the glycosylation site is required. Accordingly, one of skill in the art would not have been motivated to select the amino acid residues at positions 37, 38 or 104 for *substitution* with a cysteine residue since Wild teaches that an aspartic acid residue is necessary for removal of the N-glycosylation site and Cox teaches that *introduction* of a cysteine residue within the glycosylation site is necessary when the glycosylation site is N-linked.

The Office Action further alleges that Wild teaches modifying amino acid residues 38 and 105 results in an IL-4 antagonist that *antagonizes IL-4 activity*. However, Applicants respectfully submit that Wild is absolutely silent with regard to an IL-4 mutein that is an antagonist that inhibit IL-4 *and* IL-13-mediated activity, as required by the instant claims. Applicants further submit that, as indicated by the Office Action, Cox does not teach modified IL4 muteins. (Office Action, page 4). As such, one of skill in the art would not have been motivated to combine Wild and Cox to arrive at modified IL-4 mutein receptor antagonists that inhibit IL-4 *and* IL-13-mediated activity, as required by the instant claims.

Even if one of skill in the art were motivated to combine Wild and Cox, Applicants submit that doing so would not yield the claimed modified IL-4 mutein receptor antagonists since neither reference discloses a modified IL-4 mutein receptor antagonist that inhibits IL-4 *and* IL-13-mediated activity. Accordingly, since the combined references do not teach each and every limitation of the amended claims, Applicants respectfully submit that *prima facie* obviousness of the invention over Wild and Cox, either alone or in combination, has not been shown by the Examiner, and request withdrawal of the rejection.

CONCLUSION

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

The Commissioner is hereby authorized to charge $460.00 as payment for the Petition for Two-Month Extension of Time fee to Deposit Account No. 07-1896. Additionally, the Commissioner is hereby authorized to charge any other fees that may be due in connection with the filing of this paper, or credit any overpayment to Deposit Account No. 07-1896, referencing the above-referenced Attorney docket number.

Respectfully submitted,

Date: December 27, 2007

Antony M. Novom, J.D.
Registration No.: 45,517
Telephone: (858) 638-6641
Facsimile: (858) 677-1465

DLA PIPER US LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO CUSTOMER NO. 28213